Synthetic biology

A look through the Lens of Latin America

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Guidelines

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iGem Tec-Chihuahua

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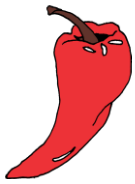
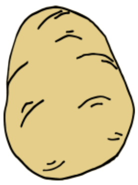
Context of Tec-Chihuahua team in iGEM 2016

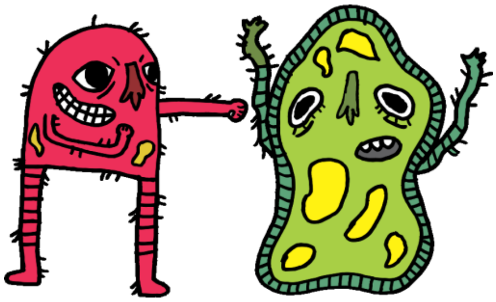
Latin American countries are some of the richest regions in natural resources in the world, thanks to which half of the economic population of these countries is engaged in agriculture. Mexico is the third largest agricultural producer in Latin America with 31% of its population dedicated to this activity. Some of the main crops found in the country are corn, sugar cane, avocado, hay, potatoes, chili and alfalfa. Talking about this last one, the production of alfalfa has a great impact locally, nationally and globally. In Mexico there are 156,141 hectares dedicated to the cultivation and production of alfalfa which produce 19.8 tons per hectare per year in average. This represents around 10.2 billion pesos in one year. The main producer of alfalfa in Mexico is the state of Guanajuato followed by Chihuahua, the big state. As the second producer, Chihuahua takes part with 12% of the national production, making around $1.2 billion pesos per year (CONAGUA, 2010).





A big part of the Mexican crop fields gets affected by pathogenic organisms, particularly fungi, which causes loss of crops. Chili, melon, alfalfa and potatoes are just a few examples. This is why fungi infections affect directly not only our state but our country by sickening the particular crop we've focused on: alfalfa. This represents not only the loss of effort, time and many cultivated hectares but also leads to great economic losses.

Due to the exposed problematic, the iGEM team from the Instituto Tecnológico de Estudios Superiores Campus Chihuahua, Tec-Chihuahua 2016 decided to take part in the competition with a project called ***Myxobacteria* as biological control method for diseases in crops**.



The aim of the project is to find a method of biological control, through genetic engineering techniques and synthetic biology to enhance the natural ability of a soil bacterium to inhibit the pathogenic fungi which causes diseases in crops. For more information about our project don't hesitate to visit our wiki: http://2016.igem.org/Team:Tec-Chihuahua

As part of the human practices area, the iGEM team Tec-Chihuahua decided to create the present brochure that addresses the background of our research and experimentation our project carried out.

After consulting almost a hundred bibliographical sources, and carrying out a deep analysis of information concerning Latin America and Synthetic Biology, this document (originally developed in English) intended by its translation into Spanish and Portuguese, works as an informative text, which allows not only the spread of synthetic biology but also the analysis of the context in which this science develops. Likewise, for those who already know or are working with synthetic biology, this document intends to expand the overview and aims to bring the reader an awareness of the dangers of the lack of information concerning Synthetic Biology.

Within the international regulatory framework there is no specific regulation for synthetic biology. This concerns not only one organization or organism but also, a whole group of them, in order to lay the foundations that can regulate the most important aspects of this science.

The aim of the Tec-Chihuahua team is to provide, through this text, a basis for the establishment of an international regulatory strategy based on Guidelines. Said guidelines derive from the understanding of the topic and reflection of a group of Latin American students concerned about biosafety and Synthetic Biology's future. iGEM's context is not limited to the laboratory work, but rather requires ethical and social considerations to evaluate the impact of the project (implemented in a real context). Therefore, the point of view of the team is formulated, since the problem to solve comes from the circumstances in which the team works and develops.

Introduction

The amounts of information generated by projects such as the sequencing of the human genome has created the necessity of handling this information in an easy way, that provided accessibility and low cost (Collins and Galas, 1993). In the past, information was limited to big research centers, and its generation depended only on having enough funding for research. The 21th century's digital era brought the opportunity to generate and handle information to any person with access to a computer. Thanks to digitalization, information is already in the public domain as an open source, allowing biology to rise (Rai and Boyle, 2007). This new perspective allowed the tendency of a larger amount of research to emerge; generating more information that is useful for making better decisions while technology advances (Cserer and Seiringer, 2009).

The pace at which technology has moved during the last few years has allowed the scientific community to understand better the genome and its functions. Originally, genes and DNA were treated simply as isolated and purified naturally occurring chemical compounds, which would make them even patentable (Rimmer and McLennan, 2012), but scientific advances to led to the change of this concept: these molecules were not *only* chemicals, they had a crucial function: carrying genetic information[1]. This new concept of genes and the interest for understanding their nature "...furnishes the very inspiration for a popular interest in genetics…" (Clarke and Parsons, 1997), and it led to the emergence of new disciplines such as genetic engineering, biotechnology, and as a result from them, synthetic biology (SB).

SB is inherently a variable and modular science which involves a naturally unpredictable area: biology and exact sciences such as chemistry, programming or mathematics in a biological engineering process (Schmidt, 2008), which implies the design and construction of parts, devices or systems, allowing the re-designing of existing organisms for a useful purpose (Desplazes, 2009). That is done through the standardization of functional parts and their insertion in "living machines", beings that can somehow operate as biological or metabolic factories (Pottage and Marris, 2012).

[1] They were actually described as "life sustaining instructions and information of the organism" according to the USPTO Applications (Calvert, 2012)

The challenge of this emerging field is not the understanding of the organisms or its processes, but rather using them effectively as productive systems to encode biological functions, (Chen *et al.*, 2012). However, these systems must be proven to work in a stable way before they can become useful. The deal with SB is that experimental results depend not only on DNA, but also on the conditions the molecule is at and its surroundings. So, working with DNA is different from working with other technologies. As referred by Giese *et al.* (2014):

> "Technology was traditionally equated with and defined by stability. Today synthetic biologists widen our concept (...) by considering both stability and instability. Instabilities are reaching the core of novel technical systems".

However, as mentioned before, synthetic biology is a multidisciplinary science that could have a broad impact in a wide spectrum of areas such as health, environment, drug delivery, renewable energy, bioremediation and industry processes[2], among others, having as main reducing costs and making procedures more efficient, which implies a strong economic impact (McDaniel and Weis, 2005; Rabinow and Bennett, 2012)

In addition, the rise of possible uses of SB has expanded the general human landscape, and that's the reason why it is necessary to reconsider the existing paradigms of science. Although it may appear like SB is a new topic, it is stated by Purnick that a "second wave" is coming, in which BioBricks (the basic units for SB) are not the key element, but rather "parts and modules need to be integrated to create systems-level circuitry" (Purnick, 2009). In other words, this second wave implies the building of complex biological systems.

Due to its complexity, SB is not as easily understood as other scientific fields are. As referred by Kwok (2010): "There are very few molecular operations that you understand in the way that you understand a (...) transistor". As a consequence, the possible side effects, achievements and limitations it brings are also harder to tackle, because programming life requires more care, control and respect than the required to program a computer. This entails that the issue should be discussed and analyzed from different perspectives. While scientists work developing the technical aspects of Synthetic biology, lawyers, economists, and philosophers deal with the social aspects that may arise.

[2] This topic is addressed in the Economy section "Biotechnology Industry" (p. 19)

Besides the increasing concerns around SB, its diffusion has become an important aspect for the international scientific community. A great part of it is possible because of the most important Synthetic Biology competition nowadays: iGEM (International Genetically Engineered Machine). iGEM started as an internal competition at MIT (Massachusetts Institute of Technology) and then evolved to a global community, being the hugest participant based *'get' and 'give'* competition" in which students from all over the world have to develop an original project based on the methodological use of standard biological parts[3]. As Smolke (2009) states, "the competition aims to shape *the ideology, values and culture of the synthetic biology community*" (Smolke, 2009) such as open knowledge, safety, security and scientific curiosity.

In the development of synthetic biology, the general scientific process acquires an element of artistic expression through the construction and design of original or creative biological systems (OECD, 2014; Jain, 2014). The possibility to accommodate scientific work under the perspective of the artistic development leads to a new concern: How to protect the final product: intellectual property or copyright?[4] Should it be patented? Is the first step ensuring the final product is stable? Because parts can be used, exchanged and modified, and therefore, the designing process would be even more valuable than the design itself.

iGEM competition has been a pioneer in these matters by breaking the rules of intellectual property and patents because *The Registry* (the main knowledge platform) and the Wikis (websites where all the projects must be shared) are free and available for participants and web surfers, making SB not only accessible but democratic.

Synthetic biology has the potential to be a keystone in science. It is a complex intersection between different disciplines availing the use of computer design and biological engineering together, making it not only integral and competent but also difficult to tackle. In spite of its "open" nature, SB is not really accessible to everyone. One clear example are the iGEM teams, most of which are located on the US, Europe and Asia; where there is enough public

[3] www.igem.org/

[4] For more, read "Law for Synthetic Biology" in the Legal section (p. 25)

and private support to finance an investigation (Burley *et al.*, 1999). Only a few teams belong to developing countries or Latin America; which leads to the question: is SB truly democratic?

Due to the issues mentioned above, it is unknown how or where synthetic biology will evolve. Up to now, discussion around SB encompasses important and varied concerns, such as security, health, intellectual property, law regulations, openness or exclusivity, economics, ethics and even playing God. There are also a lot of voices directly implied including public opinion, researchers and companies. Debates or mentions of these important issues focus on one question: What kind of science do we need? And how shall it be governed or regulated?

For Synthetic biology today's little decisions will make a huge difference tomorrow. Therefore, every risk and benefit must be analyzed for the sake of mankind. The effects in the global community shall be evaluated, and this can only be achieved when involving all subjects in a real democratic process, even those not directly related to SB, due to the fact that any collateral damage affects everyone equally. This ensures that if scientific progress is hampered, ignorance and lack of information aren't the cause of it.

The present document states a deep analysis of the context in which SB develops and the impact of three main areas. The first one is the ethical aspect in the development and advancement of science. Then, the economic repercussions from the technologies based in SB, and lastly the legal range and the international biosecurity regulations. Everything with the aim to contrast the outlook with the particular situation in Latin American countries, focused on Mexico. This because, as Gaskell (2008) said: "We can never have a science that's outside the social, and science is clearly at the heart of what we call society" (Gaskell et al., 2008).

Ethics

It is well known that one of the main aims of SB is the premise that scientific knowledge must be public and inclusive. Social interactions lead to the exchange of ideas among different individuals, but as Lentzos states "in addition to gaining access and transmitting knowledge across a generational gap, there is also a need to transmit knowledge across cultural divides between scientific disciplines" (Lentzos, 2006). Therefore, scientific knowledge is a matter concerning the whole world since scientific and technological advances have the potential to change an entire society's lifestyle and its conception of reality.

Cserer and Seiringer (2009) affirm that "the possibility of creating artificial organisms moves the basics of life reproduction into the reach of technological production", which leads to a serious ethical debate, just as it happened with cloning. Even when the main objective of SB is not *creating* life but rather enhancing life, the development of technologies based in SB will have to answer critical questions, such as: who will have access to them? Will they be open and democratic or exclusive for those with economical power? How will they impact society? And, how far would progress take society? As it is mentioned by Rabinow and Bennett (2012): "Many bioscientists hold the view that the role of ethics is principally to restrict scientific excess", which means that the possibility of exceeding the limits of nature is there.

From an ethical point of view, there are two ethical stances for the situation: utilitarianism -the benefit of the majority- and deontological perspective which evaluates morality, integrity of life and nature or the relationship between God and his creation (Heavey, 2013). As the text advances, the reader will realize it is very hard to find an unifying ethical stance. Therefore, the ethical part is tackled not from an specific stance, but rather from analyzing the main problems concerning synthetic biology.

The open biology

Openness, as defined by the Committee of Economic Development of the U.S. is "the measure of the ability to benefit from the "collective intelligence" of our world" (CED, 2006), for that reason Habermas's discourse ethics is a crucial element for the analysis. According to Berleur and Brunnstein (1996), it is based on how "individuals may become the source of a common and consensual action being morally founded through argumentative procedures". Then, deliberation is the tool by which social cooperation is achieved when every person involved exchanges their point of view, understanding, perspective and interests. This way an open-to-everyone dialogue is created. Openness is therefore based on debate, participation, democracy and consequently public discussion (Habermas, 1998).

There are two main characteristic elements of openness: accessibility and responsiveness. The first attribute focuses on increasing the access to information so that anyone -or at least a lot of people- can contribute. The second one is based on contributions and refers to the degree to which work can be modified by anyone, allowing more people to share their skills and experiences (CED, 2006).

The concept of inclusivity, which can be linked to the discourse principle proposed by Habermas justifies why a lot of voices should be taken into account on the synthetic biology debate. The discourse principle states that "norms can claim validity when meeting the agreement of all those concerned in their capacity as participants in a practical discourse" (Habermas, 1998). Discourse ethics defends a morality of equal respect and solidaristic responsibility for everybody; it does not exclude anybody. It is certainly linked to Kant's *categorical imperative*, but tackled in a universal way instead of an individual point of view.

This universality is reflected, as referred to before (p. 2), in the role of digitalization which it is key to the development of synthetic biology. The internet itself and platforms such as Wikipedia (or the iGEM wikis), where information is free and easy to obtain are proof of it. In spite of its positive aspects, one must not underestimate the disadvantages. In the case of the Internet, there is access to a lot of material; but there are also the dangers of malware,

spam, dubious reliability or poor quality information, etc. In the case of synthetic biology, there are biosecurity risks to consider, too. However, as stated by the Committee of Economic Development “we should not miss the opportunity to harvest the benefits openness might bring” (CED, 2006).

The "ethos of openness" is a concept introduced by Pottage and Marris; and it's the aim to reach it because of its deep meaning. The Greek ethos means "character", "nature" or "customs". According to the Oxford University Press, ethos is defined as "the characteristic spirit of a culture, era or community as manifested in its beliefs and aspirations" (OED, 2016). An ethos of openness implies then “the needs” of synthetic biology: free circulation of knowledge, democracy, participation and of course, inclusiveness.

Openness is compatible with SB mainly because of this science's nature: modularity. This concept (when defined in engineering terms), implies a functional unit that maintains its properties irrespective of what it is connected to (Sauro, 2008 in Calvert, 2013). As mentioned earlier in the introduction, SB nurtures itself with many different, non-related areas. Pottage and Marris state it clearly: "parts are inherently open and democratic because they have been engineered to gather a collectivity of actors around them" (Pottage and Marris, 2012).

This democracy and participation around SB directly lead to the concept of BioBricks™, defined in iGEM as "a standard for interchangeable parts to build biological systems in living cells". They consist basically of a part flanked by a prefix and a suffix. BioBrick™ parts can be assembled to form three kinds of parts: systems (that are useful, mainly, to measure), devices (such as reporters, signals, protein generators and composites) or parts that can be Ribosome Binding Sites, protein coding sequences, terminators, DNA or regulatory sequences (Baldwin *et al.*, 2015).

But why making all this so-patentable matter open? Why has the BioBricks Foundation ensured that the information needed to build BioBricks is publicly available? The answer lies within the second "natural" characteristic of SB: standardization. This was a particular problem that the BioBricks Foundation had to tackle before institutionalizing iGEM. A problem, because, as stated by Rai "in order to establish common standards, it is necessary for these standards to be open" (Rai in Calvert, 2009). The concept needed a chassis to grow into: a common-approach way of making parts, valid and applicable for everyone, everywhere. BioBricks™ modularity wouldn't exist if parts and their assembly wasn't

standardized. But of course standardization covers not only parts, but also of their quality and stability. For these essential factors, one must necessarily base the open source on the IP system. This would imply, according to Calvert, a major global change in business models (Calvert, 2012) because “the more biology becomes an information science, the more computer software scenarios become possible within biology” (Schmidt, 2008).

Openness in SB results in a win-win benefit: registry users benefit from using parts and information available in The Registry so they can design and engineer BioBricks-based biological systems. In exchange, the expectation is that the Registry users will contribute back data on existing parts as well as information and new material to BioBricks, thereby continually improving and growing this community resource (Baldwin *et al*., 2015).

This contributes in a significant way to the ethos of open access. But what about the rest of the world? The benefit lies within three main points. First of all, innovation; as stated by Rai and Boyle “a commons-based regime will result in more innovation than a private one” (Rai and Boyle, 2007). Freely available parts accelerate and facilitate the development; since they make it easier to do research by not having patents limiting the material. This encourages knowledge, education and scientific curiosity. “The object of open source biology” -state Pottage and Marris- “is to generate a collective resource from which further biological concepts and artefacts might be created. It has to be productive, and must restore or renew itself; be constantly enhanced or revitalized” (Pottage and Marris, 2012). Innovation as a result of openness has been proven by the project of open source software, in which source code is edited by and for the community of developers. According to Hilgartner “the basic normative goal of the BioBricks Foundation initiative is ‘technological progress, augmented with the goal of supporting freedom to create” (Pottage and Marris, 2012). When there are benefits and contributions with real value to mankind, there is advancement.

The second point is major acceptance from the society. The open design, construction and use of BioBrick compatible parts promote SB’s diffusion, making parts more accessible and of easy understanding for a wider range of people as time passes by. Pottage and Marris affirm that "if parts are engineered, standardized and archived in the right way, they engage the attention of people who might then begin building as well" (Pottage and Marris, 2012). Bringing openness into SB would make knowledge accessible for everybody. With accessible knowledge there are more possibilities of innovation in technologies, and as Calvert states, "technologies empower communities" (Pottage and Marris, 2012). Involving people, bringing them into science, catching their attention and encouraging them to

participate would lead to greater understanding, and consequently to broader acceptance of SB. The third and last point is related to acceptance and economic growth, which is hoped to emerge from open biology (Calvert, 2012). Openness is the base for innovation, this facilitates development and finally, commercialization. Open biology would not only diminish the concentration of property power, but also create a “diverse ecology” of benefit both public and commercial if “parts could be patented when used to produce novel materials and applications” (Endy, 2009).

Exclusiveness

Although theoretically the concept of openness is very suitable for scientific evolution, reality presents a slightly different situation. For science to be open and democratic, all stakeholders involved in scientific and technological development should have the opportunity to participate in the collective knowledge, which does not happen in reality. Factors such as geographical location, economic investment for education and research and cultural differences determine which nations make the highest percentage of scientific contributions and which are not as advanced.

The example of Latin America has already been mentioned. In 1995, Ayala stated that governments in LA were making sustained efforts to increase the investment for science, and argued that the biggest obstacle to the development of science were the lack of schools, the economic problems derived from bad internal policies or late industrialization and the high costs of equipment or appliances (Ayala, 1995). 21 Years later, the situation has improved but, there is always the possibility of a technological regression if an economic crisis or factors such as debt and corruption are present in Latin American governments. Therefore, to some extent, science is still very exclusive. Is then the ability to do science determined by the purchasing power?

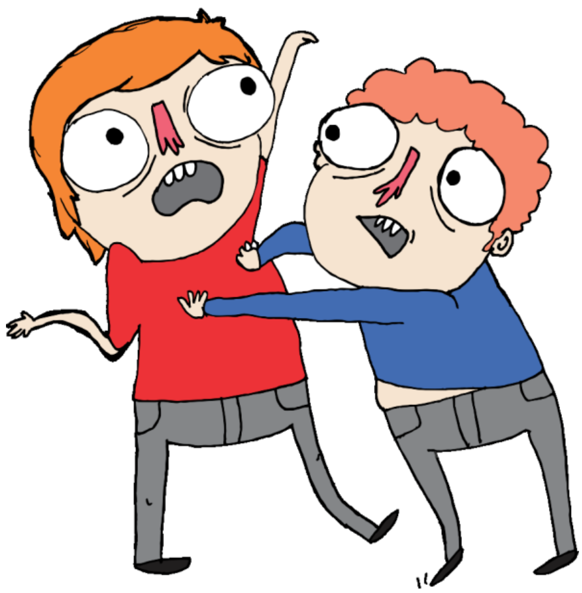
The ethos of exclusiveness is the counterpart of the open science. According to the Thesaurus online dictionary (2016), exclusiveness means “something unshared or restricted” which implies exactly the opposite of the openness principle.

The main reason why some aspects of science like the patent system in general focus on exclusiveness is because stakeholders assume that incentives are needed or have a positive impact for the well-being of the entire society. The utilitarian approach, which was developed by authors such as Oppenheim and Hettinger, affirms that “a necessary condition

for promoting the creation of valuable intellectual works is granting limited rights of ownership to authors and inventors". Absent certain guarantees, authors and inventors might not engage in producing intellectual property. Thus, control is granted to authors and inventors of intellectual property, because granting such control provides incentives necessary for social progress (Stanford's Encyclopedia of Philosophy, 2014).

The paradigm of exclusiveness implies that creators must be protected by ensuring a limited period of time in which they can exploit freely without competition their creations so they have a motive to keep innovating. The current international conventions (Paris Convention, WIPO, Copyright treaty, Patent Cooperation Treaty among others) agree with this paradigm and reinforce this understanding in the hope of achieving a major goal: *mankind progress.*

IP conflict



Synthetic Biology emerged from the mixture of biotechnology and software, both of which have had significant problems concerning Intellectual property. SB is "sitting in the intersection of two different systems of managing the creation of novelty" (Pottage and Marris, 2012). On one hand there is biotechnology, an IP saturated science where patenting is the main purpose of research. On the other side, there is the software-based approach, where openness is the aim due to its capacity of speeding up development and promoting creativity and sharing. Organizations such as iGEM, opted for openness and "although some synthetic biologists admit that iGEM is currently breaking the existing IP regime, they do not conclude from this that iGEM should modify itself in line with existing requirements, but argue instead that this demonstrates that the IP regime itself is broken and needs a fundamental overhaul" (Calvert, 2012). But the dilemma's still there: will SB bend before the existing IP system sooner or later or will this new area be strong enough to stand its ground and foster (as iGEM begun to) its own IP-rules?

First of all, one must ask, what does IP represent? Most economies nowadays are driven by capitalism where property is the most important element and the key factor is money. In this

world, “even small synthetic biology companies operate in an environment where they usually require venture capital, and as a result need to file patents to demonstrate that they are a good target for investment” (Rai in Calvert, 2009). Wealth is power; therefore, it is no surprise that science and research decisions depend on whether some study area might be profitable or not. The scarcity of freedom provoked by this economic system causes, of course, some tension between two main interests: the attribution or scientific credit, of intellectual value for every researcher and the benefit, meaning the commercial reward. This “fight” for credit obstructs the development of collaboration for the sake of science, since, as quoted on BioSocieties, “to have an IP right is necessarily to have something like the powers of control and exclusion that lawyers ascribe to property” (Pottage and Marris,2012). The “ethical repartition” of credit evolved (under pressure) to a change of the sense of scientists’ contributions; where the scientific credit became an economy of price (Pottage and Marris, 2012).

Repartition is a particular issue for synthetic biology. A multidisciplinary science necessarily requires collaboration from experts in different areas. Because of the actual system, SB is caught between the need of collaborative work and shared property and the pressure of individual property and patents to obtain economic retribution. When constructing, the part must be “a product of an ethical repartition” so that there is a balance of credit both for the individual researcher and “the whole” (Pottage and Marris, 2012). Adopting openness would mean constructing a scientific moral economy, due to the existence of the duty to share materials, constructs and procedures. This would be achieved by “recognizing the contributions of each researcher to the collective object; acknowledging the researcher’s act ‘in service of producing a larger system of knowledge” (Pottage and Marris, 2012), which is necessary for humanity to advance and achieve progress.

Progress

Progress is a key element to understand the justification behind the exclusiveness paradigm, but progress is not a quantifiable item. To achieve progress, it is necessary first to produce an advancement, because progress involves a positive change so it certainly needs a transformation. It is impossible to progress without changing for the reason that if it remains the same as before, it has not progressed by virtue of the nature of the concept (Dodds, 1973). But then, advancement implies the development or improvement of something (Cambridge online Dictionary, 2016), progress may rarely come from a technological regression (take one step backwards to take two steps forward). In this case, advancement could be seen as a major component of progress, so advancement can or cannot produce

progress but progress must almost unavoidably be preceded by advancement, which leads in turn the innovation element, associated with creativity.

Advancement is also an empirical fact which requires empirical data to be proven. “The idea that exclusive rights in new knowledge will promote scientific advancement is counterintuitive to many observers of research science, who believe that science advances most rapidly when the community enjoys free access to new discoveries” (Eisenberg, 1989).

Even if Eisenberg's premise is correct, it can lead to the remark that “over the past three hundred years, mankind has compiled an impressive record of pushing back the apparent limits to population and economic growth by a series of spectacular technological advances” (Meadows *et al.,* 1972).

Despite the fact that it is not known what kind of advancement could have been obtained if knowledge was totally open, the technological advancement in the current paradigm is certain. In the biotechnological area (and therefore synthetic biology), the acceleration of inventions and new projects has grown extremely fast as well as with The Digital Revolution (Abdelgawad and Wheeler, 2009). Up to now, The Digital Revolution has delivered incredibly useful scientific advancements in the last 20 years; Biotechnology (and associated areas) is currently still to deliver yet practical inventions (Kwork, 2010).

As mentioned above, the advancement of synthetic biology under the current paradigm of exclusiveness is undeniable. Nevertheless, as explained before, advancement does not automatically mean progress. Progress in the branch of synthetic biology demands to concur with the fundamental aspiration of technology which is, by definition, to facilitate human objectives (Thesaurus, 2016).

When looking for the general objective of humankind (detaching particular cases), is relatively easy to affirm that progress is the most important concern for humanity. But progress is a very large concept, so to effectively disclose the matter of the issue, it is

essential to look at the core values of human society, because it is in the consensus where the truth resides and is in the core of the collective principles (ethos) where the catalyst for the progressive human action inhabit. The utmost actual consensus and the preeminent collective principle in today's human society is no other than democracy.

In his book *Democracy As A Universal Value (1999),* the Nobel Prize winner and Baharat Ratna awarded Amartya Sen describes:

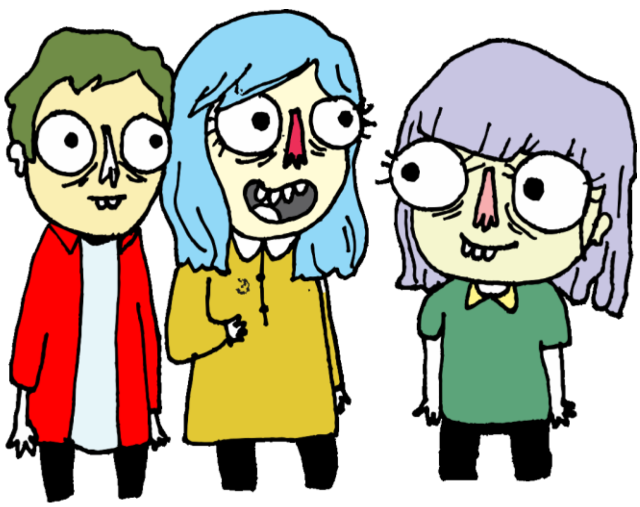
> "I was asked by a leading Japanese newspaper what I thought was the most important thing that had happened in the twentieth century… I did not, ultimately, have any difficulty in choosing one as the preeminent development of the period: the rise of democracy."

The rise of democracy and its consolidation is the most recent meaningful progress of mankind; it must be always preserved and protected, even if it means to change the current paradigms. The same source indicates that also democracy is "the preeminently acceptable form of governance" (Sen, 1999).

Professor Frank Hendricks in his book *Vital Democracy: A Theory Of Democracy On Action* states "any proposed solution can be declared bad and is set aside if labelled undemocratic", and affirms that "any problem becomes serious if it can be represented as a *problem of democracy"* (Hendricks, 2010)*,* which is the present case. Democracy is an indispensable part of progress. Humankind progress cannot happen with exclusiveness. This paradigm does not generate any real progress, just advancements. The aim with law, synthetic biology and science in general is to progress. The paradigm must change if progress is to be achieved.

Democracy

Much has been mentioned about the term democracy as a government form and as a turning point for scientific progress and open science, without deepening in its real meaning. Democracy from the latin *demos* (people) and *Kratos* (power) is more than a government system. By itself, the



concept of democracy requires a comprehensive analysis, since as a theory, it includes all the relevant conceptual aspects, but for our purposes it will be considered as democratic, the processes in which dialogue or participation intervene, including collective knowledge because as Lee and Roth (2006) state: “In a democratic society, no single form of knowledge can be privileged at the expense of other forms of knowledge” (Lee and Roth, 2006).

The same source indicates that “in a truly democratic society the common good seeks over particular partial interests” (Lee and Roth, 2006). Also, as Amy Gutmann explains, democracy also depends on “Intellectual freedom, coupled with the responsibility of individuals and institutions to use their creative potential in morally responsible ways” (Gutmann, 2011). Thus, democracy is a collective choice for science, which is reached through democratic deliberation. When applied to emerging technologies such as synthetic biology, democracy allows considering both kind of opinions: progress mediated by synthetic biology as positive and on the other side, the negative aspects because of the potential risks that it could generate (Gutmann, 2011). Maybe, like some people say “There is no progress without a risk”.

Concerning risks, Coeckelbergh affirms that “A new technology not only carries risks, it can create new ones” (Coeckelbergh, 2013). This assertion leads us to ask if there is any relationship between those risks and the fact that science is not completely open. The answer is yes: since synthetic biology could be applied to almost any area of industrial production, technological development and public services such as water treatment or health, it is thought that its impact in these areas means that anyone can access to biological and genetic engineering techniques that require more than a technical level to take place. As Kuhlau et al., (2008) says: life scientists should strive to prevent harm, within their professional responsibility, capacities and abilities (Kuhlau *et al.*, 2008). Handling life is a big responsibility that should not be taken lightly; therein lies the need for scientific development to be carried out under ethical and quality standards.

If the policy of openness were fulfilled, anyone could be an "artist of life" and numerous international regulations regarding scientific practices would be needed to prevent putting humanity and environment at risk. The debate about how such regulation should be, continues.

Weir and Seilgelid (2009) give an important perspective concerning responsibility: “Professionalization may be seen as a strategy for making scientists think and act like doctors” (Weir and Seilgelid, 2009). Because of the responsibility associated with synthetic biology, a governance strategy that has been proposed is that the development of this science could be done under oath, as it is in medicine. Thus, even if everyone had access to sources of information, the difference would be how to develop practical exercise.

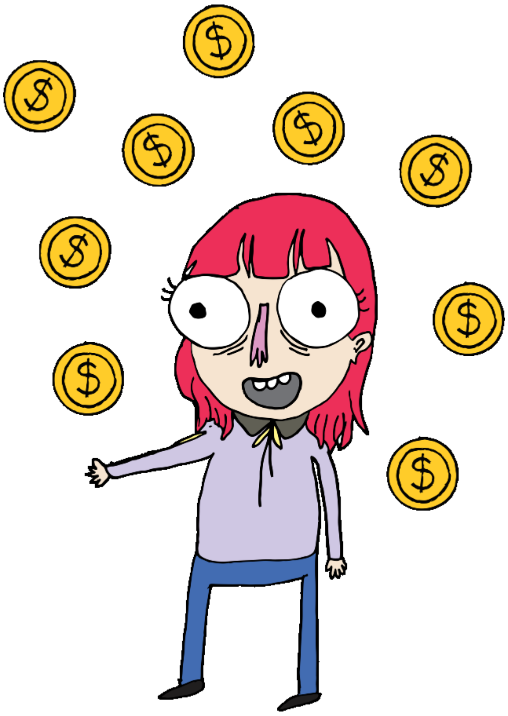
On the other hand, regulation of synthetic biology depends on participatory democracy. International meetings held on the matter must include representative minorities to take decisions concerning SB. Gaisser and Reiss affirm “The importance of efficient interactions between science–industry and government has been discussed among innovation research scholars for about 15 years” (Gaisser and Reiss, 2009), which emphasizes the need of equal participation from all sectors of the population.

However, it is important to evaluate and predict the risks of progress and the impact to the global community, which can only be achieved by giving the opportunity to include all subjects in the democratic process about synthetic biology, even those that are not directly related to scientific areas and detractors due to the fact that any collateral damage affect everyone equally. So that if something is going to hamper scientific progress it is not going to be ignorance. However, divergence that may exist between the state and the industry could have a real impact on the science.

Economy

In past years, the economy of emerging technologies could be seen from two different ways: new markets established around some type of technology or scientific development, or new markets already established requiring new specific technology. However, new economic tendencies suggest that certain emerging technologies such as synthetic biology, not only seek to be economically profitable, as Assimakopoulos *et al.* (2015) affirm, but are also looking to “demonstrate potential for increasing societal well-being” (Assimakopoulos *et al.*, 2015).

Biotechnology Industry



Biotechnology is an area whose socioeconomic scope is undeniable. It integrates theory and practice of engineering with biological sciences. As it was mentioned in the introduction (p. 4), it can be applied to a wide range of industries: agriculture, mining, food, medicine, and many more. Biotechnology became popular in the late 1970’s (ONU, 2002), although it had made its first appearance in the late 1960’s in the fermentation industries, for the fabrication of beer and cheese. With time, microbial fermentation evolved to produce ethanol fuel for agricultural purposes. This use of living beings as machines opened the way to the pharmaceutical industry, with a huge impact on antibiotics, of which penicillin is a very important example (Bud, 1995).

As it was mentioned, the application of new techniques in fields like biochemistry, molecular and cell biology opened the doors for new technologies to develop. The recombinant DNA techniques go back to 1973, but even though biotechnology was already trying to fit into the market, the rise of genetic manipulation is the factor that showed the potential of this new industry during the last decade of the XX century (Tisdell and Xue, 1999). Nowadays in the XXI century, biotechnology can enter the leading industries thanks to the recent advancements in the techniques used for genetic modifications. This circumstance has raised the interest for biotechnology from agricultural industry, with the development of

modified crops. Also, following DaSilva *et al. (1992):* “For the developing countries the potential benefits of biotechnology are significant” (DaSilva *et al.,* 1992).

Genetic manipulation methods applied to plants and crops have helped scientists to develop new plants varieties, reduce the need for pesticides, enhance the quality of the final product in the market and even transfer genes from one plant to another. However, consumers have recently developed a critical position *vis-à-vis* the products of such intervention, due to the lack of information about biotechnology and the uncertainty concerning the safety of modified products. Despite this obstacle, the industry has incorporated biotechnology as an important element for its own development (Shoemaker *et al.*, 2001).

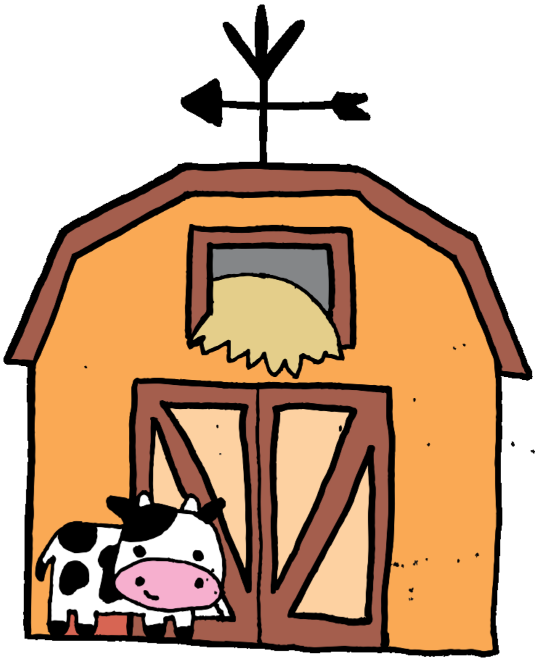
The advancements in technology can, however, affect the existing economical balances. Changes in the economies of several States cannot be completely predicted, and could be a particular risk especially for the agricultural sector in developing countries. Such changes have already been witnessed in the past decades, with both positive and negative effects on the distribution of wealth and welfare across the globe (Shoemaker *et al.*, 2001). Nowadays, research and development from both the public and private sectors have introduced synthetic biology and its immense potential. However, it is still uncertain how this novelty will affect the economies, in particular from Latin America and developing countries.

The arrival of synthetic biology

It has been discussed before synthetic biology's definition, but from the economic perspective it is not easy to define its effects on the market. One possible strategy is to use as a starting point the disciplines from which SB derives, to analyze their effects on the markets and speculate the approach needed in the industry. As a very complex technology (Introduction, p. 4), SB can be related to many different fields, but it is mainly rooted to biotechnology and mostly depends on genetic engineering, with an important role also played by software engineering (Check, 2005).

Synthetic biology is now emerging as the industry of the future due to the fact that it can make a very attractive retrenchment in production in comparison with natural manufacturing. This is mainly from the perspective of developed and industrialized countries, but the effects on some of the other developing countries might not be so beneficial, at least not in the short term.

In developing countries, the adaptation to new technologies mostly relies on how the government reacts. Governments can either facilitate a transition, embrace the new technology and profit from it, although at a very high cost, or simply leave the market unregulated and subsequently try to limit possible adverse effects. Since synthetic biology is not entering the global market, it is important to understand how the markets will behave in order to enhance the positive outcomes and diminish as much as possible the undesired ones. As a starting point, two examples of what happened to developing countries when synthetic rubber and synthetic indigo are presented (Bouchaud, 2008).



Since the 1890s the natural production of indigo represented an important share of the Indian economy. When German scientists synthesized indigo for the first time, its net price dropped by 50% and artificially synthesized indigo, produced directly in first world countries, began dominating the international market (Wellhausen and Mukunda, 2009). The Indian government, by that time still British, didn't support the producers of natural indigo to recover their stability. Eventually India ended up losing its share in the indigo market and to compensate this loss, they later changed to sugar crops. Although they got back in the market again, the transition was really difficult because of the impoverishing of the farmers.

On other hand, the production of rubber in Malaysia was not affected so negatively from the arrival of synthetic substitutes. Synthetic rubber entered the market in the middle 1950s, when the economy was dynamic and able to adapt to the new changes. Malaysia was one of the main producers of rubber and when synthetic rubber became superior in quality and performance, as well as cheaper to produce, the risks for the Malaysian economy were significant. However, the Malaysian government managed to invest into research, improving productivity and making natural rubber sustainable and competitive on the market (Hurley, 1981). As a result, the countries producing natural rubber and those manufacturing the synthetic substitute shared the market with healthy competitiveness that benefitted consumers and all the agents involved.

The differences between the way these two governments reacted to the introduction of new technologies may be influenced a little bit by the different era in which each one was presented. Even so, what needs to be learned is that if governments commit to help in the transition to new markets by investing and funding investigation, synthetic biology could become an advantage and the economic instability that this transition may cause, could be mitigated.

Being aware of what happened in the past when SB entered the market and how the situation was managed, mistakes can be avoided. Nevertheless, the future must be a concern too. Nowadays there are some other possible consequences that the economy may suffer if SB is not well regulated. There are mainly two effects that are concerning the global economic wellness: Winner takes all economy, a tendency where there's just a few or only one major winning part in the market, and Dislocation, that mostly refers to the displacement of farmers in developing countries. Both will be explained with detail later.

When only the 5% to 10% of the companies of one industry are the shareholders of most of the total value of the industry, that's called a winner takes all economy, a polarization of winners and underperformers. The winners learn to exploit the slightest advantage over the competition, which leads to big rewards (Campbell and Hulme, 2001). Patents ensure that no other actors take their advantage away. That is why we've been talking before in ethics and law about the importance of an open source.

Early and strong investors tend to become larger over time, building a monopoly. Every time these companies gain more power they have the need to start looking for more, and sometimes this means to gain their wealth at the expense of those lower on the economic ladder (Hacker and Pierson, 2011).

The new synthetic production techniques these companies propose will facilitate more opportunities for the industry. Unfortunately, at the same time they would tend to substitute the former natural methods of production, causing a displacement of traditional producers out of the market.

The optimal development for synthetic biology in the market is in the industrial appropriation of the biomass, that is to say, the primary raw material. One thing about biodiversity is that the biomass is not equally distributed in the planet, and it is mostly found in tropical countries, in the South. This could change the economic outlook for many farmers in Latin America because the strong investments on the market come from the North aiming to get this biomass for their own technologies (ETC Group, 2016).

This has been discussed earlier in the indigo case, where the indigo farmers were *displaced* from the market by the synthetic product. Maybe some other farmers will not be as lucky as the Indians that found the sugar crops, displacing them for real from the only way they knew of gaining life. In other words, synthetic production may displace some natural productions if the market is not well regulated. However, some synthetic biology derived goods increase the standard of living of these developing countries. When facing a loss and benefit situation, where the quality of life is a priority: How can a balance that benefits both parts be found?

The possibilities for the synthetic biology to fall into one or both of these problems may be a little high, but there are some ways that developing countries could try to mitigate them. Some in middle term and some others in long term. The first responsibility faced in this process of regulation is the government. Through research, education and investment, countries could be at least a little updated in science, making them strong enough to compete against the big companies and not be overshadowed by them. In developing countries, public funding and subsidies may be needed to start these kind of initiatives.

In the industry itself, if SB is seen as an advantage and not as a disadvantage, the economic stability will come along. If a new bio-synthetic product is well studied, more uses or reuses could be found in its basic parts. With more uses, the price goes lower and lower because its production also becomes cheaper; in other words, a tipping economy effect will begin (Henkel and Maurer, 2007). Instead, if it is chosen to close up to the idea of synthetic biology, the new technological findings will remain unachievable for some people or even countries. The last two hundred years the key for a technological progress has been adaptation. Adaptation to new technologies opens the door for the economy to develop in another level. If countries learn to adapt to SB instead of fearing it, the harmful effects can be mitigated while the outcome can still be beneficial.

Legal

Synthetic biology (SB) aims not only to redesign biology as a science but also to revolutionize the legal approach to technology and inventions. As explained before[5], SB with its modular, scalar structure and the accessibility of the single parts, incorporates the ethos of openness, free circulation of knowledge, democracy and diffusion of biotechnology.

The supporting technologies, the philosophy, as well as its economics, make SB a promising emerging technology. Nevertheless, all these innovative elements also make SB particularly difficult to regulate according to the existing principles and provisions of the law. The combination of paradigms of ethics, economics and technology, in fact, is proving to be difficult to translate into legal language.

Two main issues rise from SB with regard to the law: What law can be applied to SB? As explained below, SB was created as a form of Open Source technology. As such, it is hard to make SB fall within the framework of Intellectual Property Rights. Furthermore, the combination of computer science and biotechnology might represent "the perfect storm", from the regulatory perspective, for the development of SB. Therefore, the way the law regulates them can influence the regulation of SB too. The challenge is to find a regulatory solution that allows SB to maintain its openness while keeping into account the economic aspect.

In addition, organizations like the Central Intelligence Agency (CIA) and the United Nations Interregional Crime and Justice Research Institute (UNICRI) have already externalized their concerns about this emerging science. They believe that SB might contribute to the creation of more precise and lethal bioweapons as one of the science's objective is to simplify the biological/genetic engineering with the creation of standardized parts (UNICRI, 2012; CIA, 2003). Also it had been highlighted that even though an expert actor is involved in the creation of a modified organism with the use of BioBricks®, it is harder to anticipate the unintentional dangers of SB, for example mutations (Ball, 2004).

[5] See "The open biology" in the Ethics section (p. 9)

Law for synthetic biology

The aim of synthetic biology is to construct artificially programmable genome through the use of standard parts (Kumar and Rai, 2006). Thus, companies, government and private researchers desire to protect synthetic biology in the most effective way.

Synthetic biology operates with the concurrence of two fields: biotechnology and computation (Rai and Boyle, 2006). The confluence of those two disciplines sheds light onto a fundamental problem: intellectual property rights. By assimilating new technologies researchers could possibly have the risk of violating intellectual property rights; on the other hand, the limits that intellectual property law pose over new technologies could also prevent their development.

There is a conflict with the concept of “openness”: in a great majority of countries, in fact, intellectual property laws insist that innovative inventions should remain protected through exclusive rights; on the opposite side, supporters of synthetic biology advocate in favor of the creation of “public commons”, which are intellectual property rights that impose obligations of openness on future researchers, scientists or developers (Kumar and Rai, 2006). What would, then, be the ideal property regime for synthetic biology? There appears to be three types of protection regimes for synthetic biology: a) patents, b) copyrights and c) trademarks.

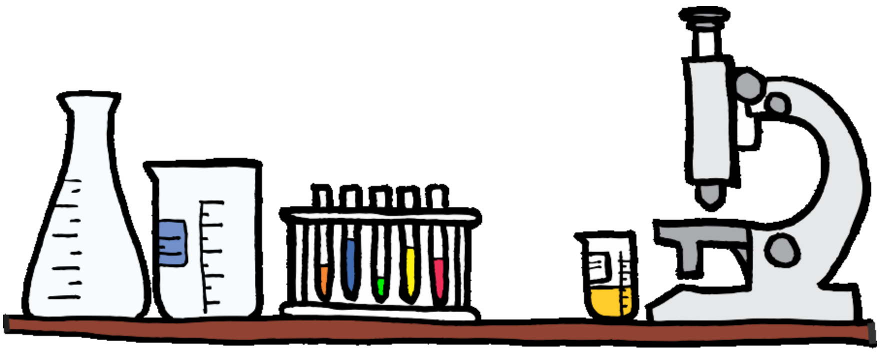
Patents have been used by many companies for the protection of synthetic biology products: the first patent with DNA as a claim element was issued in 1973. Because genes constructed through synthetic biology techniques have as their source human imagination, they do not constitute products of nature, and therefore, they are patentable subject matter (Kumar and Rai, 2006).

Patents require utility and non-obviousness, they are a property regime that excludes algorithms and formulas (Rai y Boyle, 2006). But patents are no wonder at all. Historical evidence shows that the broader the patents on foundational research, the slower the growth in the industry. Is the copyright regime, then, the most adequate for synthetic biology?

Copyrights protect original works of expression with the exclusion of works that have been regarded as functional. The discussion on the applicability of copyright law to DNA sequences and genetic arrays or materials has been discussed by many authors. The legal

concept of copyright involves "original works of authorship fixed in any tangible medium of expression, now known or later developed, from which they can be perceived, reproduced, or otherwise communicated, either directly or with the aid of a machine or device". Through synthetic biology people can design and construct new DNA sequences and can "write it" when synthesizing it, thus qualifying as original works of authorship. Furthermore, DNA and genes possess nucleotide sequences that can be determined in an easy way, and finally, DNA genetic code and arrange of genes can be reproduced through the aid of machines and laboratory methods.

In this way, synthetic biology products, such as synthetic DNA, genomes and arrays of genes could fit in the categories of literary works and computer programs (Kumar and Rai, 2006), being subjects of copyright protection.



Trademarks are useful property protection regimes, too. According to the United States Patent and Trademark Office, a trademark can be defined as a "word, phrase, symbol, and/or design that identifies and distinguishes the source of the goods of one party from those of others" (Kumar and Rai, 2006). Trademarks are useful to control the quality of synthetic biology products, as it happens in the case of the BioBrick Foundation.

A fourth alternative for synthetic biology property regimes, that does not involve any property right are contracts. A contractual focus for synthetic biology is an interesting approach because rather than having a property right as its underlying basis, a contract imposes conditions on both parties upon the sale of a synthetic biology product, where it is needed to agree on the conditions of use, distribution and dissemination of information about the product. A contractual focus is, by no means, exempt from problems: because a contract imposes conditions only to the parties bound by it, the desire to prevent leakage of information drives companies or individuals to impose strict conditions for the dissemination

of information. This undermines the development of an open approach to science advancement.

What would, then, be the ideal form of property protection regime for synthetic biology? As one can see, each and every property regime has both benefits and disadvantages. First, patents, on the one hand, through the Copyleft license, allow other people or companies to make improvements to a product with the condition of making public those improvements again. On the other hand, the cost of a patent is usually expensive, costing in the United States, for example, up to $25,000 USD per patent for complex inventions (Kumar and Rai, 2006). Second, copyrights are attractive. On the one hand, copyrights are generally inexpensive, they attach to an author's work immediately upon creation, the term of protection is generally long, and they provide a perfect basis for Copyleft licenses. On the other hand, the legal basis of assertion of copyrights is unclear, at least in the United States. Third, trademarks are useful, but in some countries are expensive and are considered as the weakest form of intellectual property regime as it protects marketing concepts of products while having a weak range of protection over the product itself.

Fourth, contracts are very useful property protection regimes; contracts are not only inexpensive, but as the terms of every contract can vary, they adjust well to the needs and concerns of both of the parties. An important disadvantage, unfortunately, is that contracts are often subject to strict requirements and regulations for the dissemination of information, which creates a close system instead of an open one.

Synthetic biology commons appear to be one of the answers that scientists have found to the problem of property regimes. BioBrick Foundation (BBF) both as the iGEM Competition have been the first ones to promote openness in the field of synthetic biology.

The BioBrick Foundation was created by MIT scientists and operates under the principle of open source, which allows further researchers to modify, redistribute, and improve the source code freely. In order to fit into the Open Source Definition (OSD) synthetic biology products must meet the requirements of a) being freely distributed, b) the source code must be available, c) the redistribution of derivative works must be free, d) non-discrimination against potential users or fields of use and e) technology must be neutral.
From all of the above a conclusion can be reached: too much protection can deter research and restrain scientific development in the biotechnology sector. An excess of intellectual property claims in a specific field can produce what has been called by some authors the

“tragedy of the anticommons”, where the proliferation of too many ownership claims over a resource makes it impossible for anyone to use it (Rai and Boyle, 2006).

Security risks

Along with the wonders of synthetic biology come the inherent biosecurity concerns. The risks connected to SB revolve around two main issues. If the SB continues to develop, it might achieve its purpose of redesigning biological sciences into simpler disciplines granting the possibility to people with no expertise in the area (hereinafter referred as “non experts”) to develop this technology. In addition, SB is intended to incorporate the ethos of openness and free knowledge circulation mainly by the register of standardized parts making them relatively easy to acquire. Consequently, the first issue is that SB might be giving the perfect and easier tools for a person or group to create/improve a bioweapon or commit an act of bioterrorism. As explained Serrano (2007): “The main concern in Biosecurity arises however from the possibility that rogue states or terrorist’s organization re-engineered microorganisms, or living systems with the purpose to harm” (Serrano, 2007). Therefore, an important question to formulate would be: how can governments avoid bioterrorism while keeping into account openness?

It seems senseless that human beings have a destructive potential capable of harming himself, however, risks depend not only on bad intentions. It cannot be ruled out the possibility of collateral damages (Gutmann, 2011). Likewise, to understand the magnitude of the second issue, it is necessary to scheme SB on a larger picture where it has continued to grow to large industrial volumes (Moe-Behrens, 2014). In this scenario, a large number of synthetic organisms would be released into the environment, but what if the scientific community is not able to control them? Is there a way to anticipate the unintentional dangers of synthetic biology? Both of these issues and its questions will be analyzed at this section of the paper.

While dealing with the same thing in essence there is a conceptual distinction between biosafety and biosecurity. As Kelle (2009) explains: “While a biosafety risk classification system is based on the inherent capability of [microorganisms] to cause disease, of greater or lesser severity, in humans, animals and plants, a biosecurity risk classification system is founded on the potential of a [microorganism] or toxin to be used as a weapon” (Kelle, 2009).

Bioterrorism

In 2002, virologist Eckard Wimmer demonstrated at the State University of New York how impressing the potential risks of synthetic biology can be by presenting a live poliovirus. This microorganism was created by his team from scratch using only DNA segments freely available on Internet and that could be ordered via mail. The problem that was highlighted with the demonstration was the lack of biosafety regulations and, therefore, the potential risks of synthetic biology mentioned above (Ball, 2004).

In other words, if synthetic biology succeeds in its purpose of lowering the complexity and exclusivity of biological technology, a wide range of biotechnological capabilities might become more accessible to non-experts. This may translate to a negative effect of making bioweapons easier to acquire or build, cheaper, and making them more controllable and effective on their intended negative impact (UNICRI, 2012).

Experts believe that there might be a wide range of potential perpetrators with different motivations to use synthetic biology or nanotechnology. This with the purpose of creating or modifying agents that could be used as weapons (UNICRI, 2012). For example:

- Terrorist Groups: Terrorist groups might consider the use of advanced biological weapons compared to both traditional agents and conventional weapons as they have a certain number of desirable characteristics. For example, an advanced bioweapon might increase the potential impact of an attack inducing a complete population to fear and undermining their faith in the ability of its government to protect them. Nowadays the bioweapons are limited by their complexity, the lack of easy obtainable resources and the amount of time required. However, synthetic biology might enable the acquisition and use of these type of weapons (UNICRI, 2012).

- Religious Sects: Extremist religious sects in particular occasions have the desire to act in the name of God. The notions of “playing God” are imminent in synthetic biology and nanotechnology. The secular philosopher of law Ronald Dworkin use the expression ‘‘playing God’’ in the biopolitical discourse. Drees (2002) in Dabrock (2009), accuses everyone using this phrase of being intellectually and morally dishonest. He agrees with Dworkin that ‘‘playing God’’ is an indirect expression of strong concern towards the use of power and its consequences. The manipulation of

life is exceedingly serious and it should be handled with great care (Baldwin *et al.,* 2016). Dworkin attributes this to the observation that the undermining of old established cultural structures does not only lead to changes in the image of man, but also in the image of God. This might increase the probabilities of a sect choosing to use a bioweapon (Dworkin, 2000; Dress, 2002; Dabrock, 2009; UNICRI, 2012).

- Organized Crime: Synthetic biology might help improve the metabolic pathway approaches by making them cheaper and increasing their production in less time. The organized crime then might use or develop economic incentives for SB to produce narcotics, drugs or other pharmaceuticals more easily and, therefore, creating a black market for synthetic biology products (UNICRI, 2012).

- State programs: Also there is even a threat of biological weapons programs run by the State taking advantage of the advancements of nanotechnology and synthetic techniques. These programs might have the objective to seek for international powers with the creation of special operations or mass assassination weapons. This theory might lead to a biological arms race between different States around the world (UNICRI, 2012).

Although all of the perpetrators mentioned above are inferred from a hypothetical scenario, this future might not be too distant. The emergence of do-it-yourself (hereinafter referred as DIY or Biohacking) biology communities and the growth of the number of students registering for the iGEM competition might allow us to infer that SB is accomplishing its objective of being an Open Source biotechnology as the protocols of how to realize certain biotechniques are being reached by more people. It is mandatory to clear the fact that, nowadays as SB has not fully developed, it's really complicated to carry out a complete project at a DIY laboratory or at the iGEM competition having no prior background on biology at all. To work on either of the situations, it's necessary a collective expertise or receive a considerable guidance from a senior faculty member (Jefferson, 2014).

Nevertheless, not only Biohacking communities and iGEM are increasing its number of users but also their number of kits to carry out biological techniques. The actual problem is the way some organizations manage their distributions. On one hand, iGEM as a competition mainly for undergraduate students theoretically distributes its kits to socially/ethically responsible organizations ergo universities. On the other hand, there are DIY communities that freely distribute their DNA kits without taking into account the user's profile.

For example, The Odin is a small company that encourages the Biohacking movement by selling a wide range of products at an affordable price compared with those of the large companies. Their products go from complete gene engineering kits, laboratory material and enzymes to even bacteria plasmids. Even though the company is supporting the ethos of openness from the SB by publishing some tutorials or protocols and recommending some online courses, the company has no restriction on who can or cannot acquire their products. This can be proved in the checkout process when the user is requested to fulfill the billing details such as email, complete name, address, etc., like in an ordinary online shopping process. In addition to the simplicity of the registration process, the web page, even gives the option to continue as a guest without the necessity of registering. Furthermore, the consumer has no necessity of providing The Odin with any additional information. Therefore, any person (civil or terrorist) can easily acquire any product.

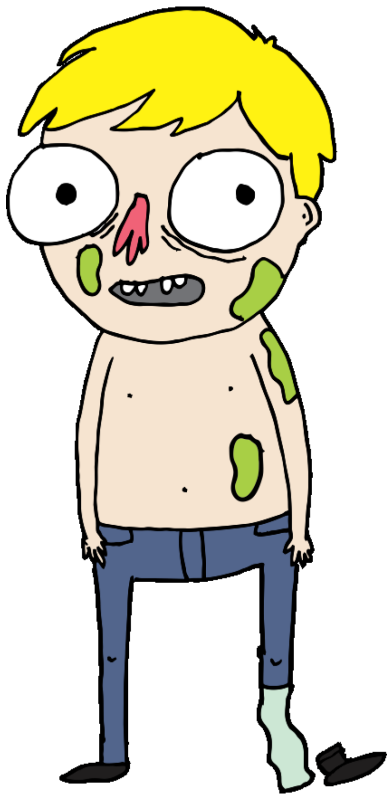
Taking into account every aspect previously analyzed, this far, it is safe to affirm that governments should address the problem that free circulation of knowledge and materials might represent in a future. As the literature suggests, there might be two main ways to accomplish this. First of all, when an individual makes an approach to a new science aiming to develop an experiment or project it is a key prerequisite to be aware of the relevant issues that revolve around the subject[6] (Kelle, 2009).

As of now, it can be generalized by saying that almost every approach made to SB involves the scientific community, however that does not imply that they are totally aware of security issues. In 2004, the Fink Committee (officially called the Committee on Research Standards and Practices to Prevent the Destructive Application of Biotechnology) published a report outcome of the increasing concerns in the USA that life sciences might be misused. Notwithstanding, interviews made to 20 of the leading European synthetic biologists between June and October of 2007 pointed out that only seven out of 20 researchers had heard of the work while only one of them was able to discuss the subject (Kelle, 2009). If even the community that is directly involved is unaware about SB biosecurity issues, then this demonstrates that there is a lack of an effective strategy of diffusion. Governments need to make an effort to raise awareness and educate people about what SB means and implies. This may assuage the fear and clear the myths not only from the scientific community but also from the general population.

[6] As mentioned in the “Democracy” issue in the Ethics section about the medical oath (p. 16)

Secondly, it is mandatory that in biosecurity regulation governments make obligatory for DNA synthesis or Chemical companies to avoid unintentionally aiding the misuse of biotechnology. Blue Heron, for example is already cross checking all of its orders for DNA synthesis with a database catalog as “biological nasties.” The company might walk away from some business if there is a match with the catalog and the customer cannot be easily checked out (Ball, 2004). Blue Heron’s company policy should be a norm that applies for everyone even with the DIY companies.

Involuntary effects of Synthetic Biology



When working with SB, it is harder to anticipate any unintentional effects. For example, bacteria with too many DNA modifications might develop unprecedented capabilities that comprise the ecosystem. This problem is hard to resolve and translate it into legal language, but the lack of an effective regulation of SB has led the scientific community to develop projects without any guidelines that ensure the safety of their product, and without the necessity to notify any authority with a safety report on their research (Ball, 2004).

As an example, the iGEM competition[7] was held for the first time as a local contest at the Massachusetts Institute of Technology (MIT) in 2003. Since then, the competition has become the most important in the synthetic biology area with more than 300 teams from all over the world. Nevertheless, it wasn’t until the 2008 edition that participating teams were required to answer a set of four mandatory questions as a prerequisite for them to qualify for a medal. Those questions were relatively simple and addressed topics such as: “safety issues raised by the project”, “the existence of safety regulation”, “the review of the project by a local biosafety group”, and the “safety assessment of the submitted BioBrick parts.” Since then the questionnaire started changing gradually. In 2010, the questions became more specific and a new ones were added regarding how to tackle safety issues that could be useful for future iGEM editions, but in spite of that iGEM competition still does not allow its contestants to realize their experiments *in vivo* (applying it in the field), only *in vitro* (which means in the laboratory) (Schmidt, 2008). Actually, on the medals’ guidelines is specified that the contestant must not

[7] Previously mentioned in the Introduction (p. 4)

effectuate any experiment *in vivo,* otherwise they will be disqualified. It can be inferred that this a security policy to avoid any problem regarding the epigenetics of modified bacteria's freed in any environment.

Some experts recommend the adaptation of some methods of biocontainment to help regulate the safety in open synthetic microorganisms. One clear example of containment is through engineered auxotrophy. This method implicates to modify bacteria through genetic engineering protocols to inhibit them to synthesize an essential compound required for their existence. These organisms will work only in a controlled environment where that compound is provided; if a bacteria escapes from there it would rapidly die (Moe-Behrens, 2014).

Another common way of biocontainment is through induced lethality where a sort of "kill switch" mechanism has been engineered as a safety measure. Toxic genes, for example, are added to a bacteria's genome and their expression is kept under control by an inducible switch called promoter. Basically, the microorganism survive normally until the promoter is induced and the toxic gene starts to produce itself killing the bacteria (Moe-Behrens, 2014).

Both are possible procedures that might be the correct answer for one of the main issues of SB's biosecurity. However, they must be adapted to improve their effectiveness on killing the host organism. Scientists need to ensure that lethal genes will not deactivate when DNA is replicating, or when any other cellular biochemical reaction takes place (Moe-Behrens, 2014).

Guidelines

As stated in the beginning the purpose of this article is to suggest a number of guidelines that can be useful for international regulation of synthetic biology. Such guidelines are proposed after the literature review of several authors, as a consensus of ideas that would be the most important points to be considered about synthetic biology.

The establishment of these guidelines as a consensus method is a procedure that other disciplines such as medicine still valid. Flink (1984), explains that medicine goes even further by analyzing specific cases and then establishing those guidelines. “When properly employed, consensus strategies can create structured environments in which experts are given the best available information. This allows their solutions to problems to be more justifiable and credible than otherwise” (Flink, 1984).

We know that Synthetic Biology is a new science so there may not exist specific cases to be analyzed in which we can base to create guidelines that would allow to prevent mistakes in the future. But this, far from being a problem, is a very positive aspect. Before having undesirable consequences, we can establish the basis for proceeding correctly in the development of synthetic biology, knowing that it is a science that will be very important in coming decades.

The establishment of international codes and guidelines is important because as Selgelid (2009) says: “Though self-regulation via codes of conduct may reduce government interference with science, the government may, nevertheless, still have an important role to play in the regulation of dual-use science in particular” (Selgelid,2009). Thus democracy and inclusion is achieved as discussed above.

In the same way, to have a regulation would ensure that the development of research based on synthetic biology will have the importance it deserves, preventing scientific work related to it from being taken lightly. People who develop synthetic biology have in their hands a great responsibility so they should be aware of it and, just as medical ethics is submitted to an Hippocratic oath (Miles, 2005), scientists should do the same. The equivalent of this oath then would be the Guidelines presented below:

Guideline 1.

Statement: Synthetic biology ought to be open in order to:

- **Allow the free circulation of knowledge and make information accessible**
- **Promote active participation and inclusion: Increasing dialogue, debate and public discussion, as well as sense of responsibility**
- **Reach universal standardization valid and applicable for everyone**
- **Trigger a broader use of information and growing the community resource with contributions, sharing of skills and experiences**

Explanation: It provides several benefits like:

a) Innovation. Freely available parts accelerate and facilitate development

b) Encouragement of scientific curiosity. Achieve technological progress by supporting the freedom to create

c) Broader acceptance from society. Diffusion engages the attention of people who might begin building.

d) Economic growth and diverse economy. Parts could be patented when used to produce novel materials and applications.

Guideline 2.

Statement: Synthetic biology should be an inclusive process

Explanation: The consequences of any process related affects everyone equally. In the decision to establish criteria, synthetic biology must have an equal number of representatives per nation and these people must include both the scientific community and the agencies that regulate and manage a global consensus as the UN, as well as members of society in general.

Guideline 3.

Statement: iGEM parts should be used for research and under a contract regime.

Explanation: There should exist contracts with lock box date where the owner compromises to donate its parts to public domain after some fixed number of years. The contracts should have a duration according to the research process, whose period may not have lucrative purposes.

Guideline 4.

Statement: It is necessary to maintain quality standards

Explanation: The quality of both the process and the bioparts deriving from the process should be subject to international quality standards. An open biology allows information to improve and renew itself; this can be achieved by standardization and requirements' fulfillment. Parts shall be tested and added to the Registry depending on their stability, effectiveness and functionality.

Guideline 5.

Statement: If IPR are necessary, Copyright could represent a valid alternative to patents.

Explanation: Copyrights are a great alternative form of intellectual property protection due to its relatively low cost compared to other forms, but they should be treated carefully. Length of duration of copyright protection in the field of synthetic biology should be adjusted to enough time for a researcher to obtain profits, but not to a long period of time that impedes scientific development.

Guideline 6.

Statement: Researches shall be financed mainly by public funds

Explanation: Public founding independent from government in order to avoid monopoly should be implemented. Such funds would be managed by an international organization and granted to research that would previously be evaluated in aspects such as its impact, quality and research process.

Guideline 7.

Statement: Synthetic biology and projects derived from there should not be used for criminal, harmful purposes or biological weapons

Explanation: Synthetic biology should benefit mankind and not be used for purposes that violate human rights or human dignity.

Guideline 8.

Statement: Every biotechnology advance must be aware of its impact on the environment. Products cannot be contrary to human health.

Explanation: Any project derived from biology should be based on the principles of scientific ethics and environmental safety. The impact on the environment and human health from each project MUST be assessed before it is approved to continue.

Guideline 9.

Statement: People or organizations who make use of parts and bricks shall be periodically verified and included in a register of controlled and safe subjects.

Explanation: Researchers and developers should not have criminal records or ties to organized crime or terrorism.

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